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Age-related changes in the functional neuroanatomy of overt speech production

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Abstract

Alterations of existing neural networks during healthy aging, resulting in behavioral deficits and changes in brain activity, have been described for cognitive, motor, and sensory functions. To investigate age-related changes in the neural circuitry underlying overt non-lexical speech production, functional MRI was performed in 14 healthy younger (21–32 years) and 14 healthy older individuals (62–84 years). The experimental task involved the acoustically cued overt production of the vowel /a/ and the polysyllabic utterance /pataka/. In younger and older individuals, overt speech production was associated with the activation of a widespread articulo-phonological network, including the primary motor cortex, the supplementary motor area, the cingulate motor areas, and the posterior superior temporal cortex, similar in the /a/ and /pataka/ condition. An analysis of variance with the factors age and condition revealed a significant main effect of age. Irrespective of the experimental condition, significantly greater activation was found in the bilateral posterior superior temporal cortex, the posterior temporal plane, and the transverse temporal gyri in younger compared to older individuals. Significantly greater activation was found in the bilateral middle temporal gyri, medial frontal gyri, middle frontal gyri, and inferior frontal gyri in older vs. younger individuals. The analysis of variance did not reveal a significant main effect of condition and no significant interaction of age and condition. These results suggest a complex reorganization of neural networks dedicated to the production of speech during healthy aging.

Keywords: Healthy aging; Speech; Plasticity; Reorganization; Functional magnetic resonance imaging; Brain; Cortex

1. Introduction

Due to modern advances in healthcare, elderly individuals are a rapidly growing proportion of the population in industrialized nations. Considerable efforts are under way to understand the mechanisms of aging better and to unravel novel approaches to modify the aging process. Traditionally, normal aging has been regarded as an inevitable decline of cognitive, motor, and sensory functions, accompanied by brain atrophy and neuronal loss (Reuter-Lorenz and Lustig, 2005). Recently, converging evidence has suggested that age-related changes in behavior, brain structure, and brain function might be far more complex than previously thought. With the advent of functional brain imaging, in particular positron emission tomography (PET) and functional

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magnetic resonance imaging (fMRI), it has become possible to compare brain activity associated with cognition (for an early study, see Grady et al., 1994), sensory processing (e.g., Cerf-Ducastel and Murphy, 2003), and motor tasks (e.g., Ward and Frackowiak, 2003; Heuninckx et al., 2005; Riecker et al., 2006) between younger and older individuals. In many of these studies, brain function of older participants has been characterized by overactivation in parts of the neural circuitry under investigation when compared with younger adults. These changes may result from neuroplastic changes in the aging brain that compensate for loss of sensorimotor function and contribute to maintaining of behavioral performance (Reuter-Lorenz and Cappell, 2008).

Speaking is one of the most complex and important human skills. During speaking, phonological plans are formed and executed at 5–10 syllables per second, using approximately 100 different muscles. In a previous study of younger adults, aged 22–32 years, we identified a large-scale articulophonologic network that mediates speech production (Sörös et al., 2006b). In younger adults, overt production of the isolated vowel /a/ was associated with the activation in bilateral cortical and subcortical motor centres. Activated cortical motor areas included the primary motor cortex, supplementary motor area, and cingulate motor area. Subcortical activation was found in the thalamus, globus pallidus, and putamen. These areas, together with their extensive interconnections, constitute the neural circuitry that controls initiation and execution of articulatory movements. In addition, production of an isolated vowel was associated with the activation in the bilateral superior temporal gyrus, reflecting phonological processing. The production of the polysyllabic utterance /pataka/ was associated with additional activation in the bilateral cerebellar hemispheres, which are crucial for the control of sequential movements. The production of polysyllabic utterances was also associated with stronger activation of the bilateral temporal cortex, reflecting an increase in phonological processing compared to the production of an isolated vowel.

Many older individuals experience difficulties and breakdowns in speech production, such as reduced speaking rate (Searl et al., 2002) and increased durations of segments, syllables, and sentences compared to younger adults (Smith et al., 1987). These age-related impairments in speech production are likely related to a decline in oro-facial motor control, as shown by decreased accuracy of movement amplitudes and increased temporal variability of movements (Ballard et al., 2001), as well as impairment of phonological processing, in particular the sequencing of phonological units (MacKay and James, 2004). Based on these behavioral findings and the results of previous functional brain imaging studies in younger adults, the aim of the present study was to compare the neural correlates of overt speech production between healthy older and younger adults using simple non-lexical utterances with varying complexity.

To study potential age-related changes in the neural correlates of speech production, whole-brain, blood-oxygenation dependent (BOLD) fMRI at 3 T was used. To minimize artifactual fMRI signal changes due to motion-correlated movements of the head and of the articulatory organs (Birn et al., 1999), clustered image acquisition (Edmister et al., 1999; Sörös et al., 2006b) was performed. Rather than the typical fMRI experimental design in which images are acquired repetitively at fixed time intervals, clustered acquisition leaves an extended silent interval for speech production and permits detailed scanning of the brain 5 s later (Gracco et al., 2005; Sörös et al., 2006b). Not only does the approach separate the rapid onset and offset of articulatory movements (and potential motion artifacts) from the comparatively slow rise of the BOLD signal (Birn et al., 2004), but the acoustic noise associated with imaging is also separated such that it does not have the potential to distract behavioral performance.

2. Methods

2.1. Participants

Blood oxygenation level dependent (BOLD) fMRI was acquired in a group of healthy younger volunteers (7 women, 7 men) with an average age of 25 years (range: 21–32 years) and a group of healthy elderly volunteers (7 women, 7 men) with an average age of 71 years (range: 62–84 years). All participants were right-handed and fluent speakers of English. Before inclusion into the study, volunteers were screened during a telephone interview for the past and present medical conditions, medication and drug use. Individuals with untreated vascular risk factors (including arterial hypertension, diabetes, hypercholesterolemia), disorders of the central nervous system (including stroke and dementia), psychiatric disorders, and hearing impairment were excluded as well as individuals taking psychoactive drugs. Volunteers were recruited with the help of the Rotman Research Institute volunteer database and by personal communication. The study was approved by Research Ethics Boards at Sunnybrook Health Sciences Centre and Baycrest. Informed written consent for participation in the project was obtained from all participants according to the Declaration of Helsinki. Parts of this study were published as an abstract (Sörös et al., 2006a), and the fMRI data of 9 young volunteers were reported in an earlier paper (Sörös et al., 2006b).

2.2. Experimental tasks

Participants were asked to repeat acoustically presented simple speech sounds of varying complexity in the silent period between fMRI data acquisitions as described previously (Sörös et al., 2006b) (Fig. 1). The required speech sounds were the vowel /a/ and the polysyllabic utterance /pataka/. Instructions were “say ah” (for the /a/ condition), and “say pataka” (for the /pataka/ condition). Instructions were transmitted through an fMRI-compatible audio system with acoustically padded headphones to reduce acoustic

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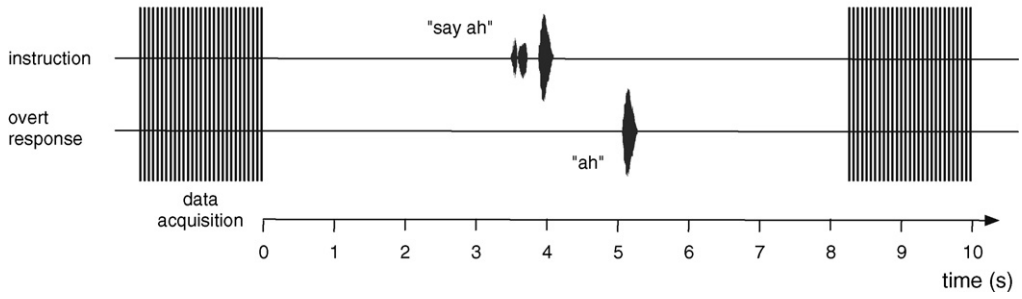

Fig. 1. Timing diagram of the experiment. Functional MRI is performed using clustered image acquisition with a TR of 10 s. Both the auditory cue and the verbal response fall within the silent interval between multislice data acquisition. The speech waveforms represent the instruction (upper trace) and the overt response (lower trace), recorded by an fMRI-compatible microphone.

fMRI noise by 25 dB (Silent Scan, Avotec, Stuart, FL). All instructions were spoken by a speech-language pathologist in a sound-attenuated room, digitized at 22,050 Hz and stored as a digital sound file. Instructions were delivered at a constant onset-to-onset inter-stimulus interval of 10 s with the stimulation software E-Prime 1.1 (Psychology Software Tools, Pittsburgh, PA). Participants were asked to produce the required utterance once, immediately after the end of the instruction. Six experimental runs were performed (1 older participant had to terminate the experiment after run 5). The baseline was 90 s in duration and interleaved throughout, consisting of 9 functional brain volumes acquired without a preceding verbal cue and without response. During the entire experiment, fMRI data for 60 spoken responses per speech condition (60 utterances of /a/ and 60 utterances of /pataka/) were collected. To minimize task switching effects, a blocked presentation of five identical cues was chosen. All instructions were delivered and all responses were made within the silent interval between the acquisition of the fMR images.

2.3. Image acquisition

Imaging was performed on a 3 T MRI system (Signa 3T/94 hardware configuration, VH3/M4 software configuration; GE Healthcare, Waukesha, WI) with the standard quadrature birdcage head coil and padding by foam cushions to restrict major head movements. For BOLD fMRI, T2*-weighted functional images were acquired using a spiral-in/out pulse sequence (Glover and Law, 2001) (TE 30 ms, flip angle 70°, matrix 64 × 64, FoV 20 cm × 20 cm, 26 axial slices 5 mm thick) that decreases signal drop-out in regions with large magnetic susceptibility gradients (Preston et al., 2004). High-order shimming was performed at the beginning of the fMRI experiment for each volunteer. Clustered image acquisition was implemented with a TR of 10,000 ms, and the data from all slices were acquired in 1800 ms of this time interval. High-resolution, T1-weighted images (3D Fast SPGR, TR 7.2 ms, TE 3.1 ms, IR-prepared TI 300 ms, flip angle 15°, matrix 256 × 256, FoV 22 cm × 22 cm, 124 axial slices 1.4 mm thick) were acquired for structural reference. In addition, T2-weighted (spin-echo, TR 3200 ms, TE 85 ms, matrix 256 × 256, FoV 22 cm × 22 cm, 32 axial slices 4 mm thick) and proton density-weighted images (spin-echo, TR 3200 ms, TE 18 ms, matrix 256 × 256, FoV 22 cm × 22 cm, 32 axial slices 4 mm thick) were acquired for the identification of potential brain lesions. The severity of white matter lesions was classified as grade 0 (absent), grade 1 (punctate), grade 2 (early confluent) and grade 3 (confluent) (Schmidt et al., 2003) by a certified neurologist (P.S.). White matter lesions were present in 11 older individuals (early confluent periventricular lesions in 2 individuals, single periventricular lesions in 9 individuals), but in none of the younger participants.

2.4. Image analysis

Analysis of fMRI data was carried out in a multistage process using the software library FSL (http://www.fmrib.ox.ac.uk) (Smith et al., 2004). An independent component analysis was performed using MELODIC (Beckmann and Smith, 2004) to investigate the presence of artefacts. Components containing artefacts due to head movement or magnetic susceptibility, but not revealing expected brain activation, were removed from the original data set, as described previously (Sörös et al., 2008). The resultant datasets were used for later general linear modelling. Linear registration and correction of head motion was performed. The maximum head displacement with respect to the reference image and the relative voxel displacement were calculated. The mean absolute voxel displacement, relative to the reference image, was significantly different but low in both groups: 0.16 ± 0.08 mm in the younger and 0.26 ± 0.08 mm in the older participants ($P = 0.002$, t-test).

Brain segmentation and removal of non-brain tissue was achieved by BET (Smith, 2002). Spatial smoothing using a Gaussian kernel of 5 mm full-width half maximum and a mean-based intensity normalization of all volumes by the same factor were applied before the statistical analysis. The six fMRI runs obtained for each participant were then analyzed independently using general linear modelling. Independent analyses of each run were chosen to avoid artefacts related to motion correction and filtering. Statistic

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parametric (Z score) images were thresholded using clusters determined by $Z > 2.3$ and a (corrected) cluster significance threshold of $P = 0.05$. Because of the long TR no temporal auto-correlation was assumed between images of one volume and another.

A generalized mixed-effects analysis was then carried out to analyze effects across the 6 runs using FLAME (FMRIB's Local Analysis of Mixed Effects) with $Z > 2.3$ and a (corrected) cluster significance threshold of $P = 0.05$. Cluster-thresholded activation maps were registered to the high-resolution T1-weighted image. Finally, a mixed-effects analysis was performed across all participants with $Z > 2.3$ and a (corrected) cluster significance threshold of $P = 0.05$.

A two-way analysis of variance (ANOVA) was performed within FSL to test for the main effects of condition (/a/ vs. /pataka/) and age (young vs. old) and the interaction condition × age. For visualization, Z-statistical maps were overlaid onto a three-dimensional reconstruction of the MNI 152 standard brain provided by FSL. The reconstruction of the brain's surface was performed with FreeSurfer (http://surfer.nmr.mgh.harvard.edu/) (Dale et al., 1999). The anatomical labels of activated brain regions were retrieved using FSLView 3.0 (http://www.fmrib.ox.ac.uk/fsl/fslview/index.html).

2.5. Sample size and statistical power

To estimate the sample size necessary to achieve an 80% power in our study, we used the results of two papers that performed simulation experiments and analyzed data of real fMRI experiments (Desmond and Glover, 2002; Hayasaka et al., 2007). In the study of Desmond and Glover (2002), about 12 subjects were required to achieve 80% power at the single voxel level, based on parameter estimates from a verbal working memory experiment. Similarly, the study of Hayasaka et al. (2007) found that approximately 13 subjects would be required to achieve an 80% power in an auditory stimulation experiment. These papers, however, estimated sample size and statistical power for within-group analyses. In our study, we performed within- and between-group analyses. To estimate the necessary sample size for the between-group analyses in our study, we referred to the sample sizes of studies comparing movement-related hemodynamic responses between younger and older participants. A systematic literature search identified 10 studies that directly compared movement-related BOLD responses between younger and older participants. Nine of these studies studied 13 or less individuals per group (Fang et al., 2005; Heuninckx et al., 2005, 2008a; Hutchinson et al., 2002; Mattay et al., 2002; Onozuka et al., 2003; Riecker et al., 2006; Taniwaki et al., 2007; Wu and Hallett, 2005). Only one study investigated more than 13 individuals in one group (12 younger vs. 26 older adults) (Heuninckx et al., 2008b). Based on the sample sizes of these studies and their ability to identify age-related differences in motor control, we are confident that our group sizes (14 younger vs. 14 older adults) are sufficient to perform a direct comparison of brain activation associated with speech production in younger and older adults.

2.6. Recording of behavioral responses

Jaw movement was monitored using a flexible, fMRI-compatible fiber-optic joint angle sensor (S700 ShapeSensor, Measurand Inc., Fredericton, NB, Canada), attached to the chin and chest of the volunteer. Bending of this sensor modulates the light flux through the sensor. The intensity of the returning light signal was digitized at 40 Hz and recorded using a custom-written Labview program (National Instruments, Austin, TX). Collection of joint angle data and fMRI acquisition were synchronized by E-Prime. The onset latency and the amplitude of jaw opening were calculated using a custom-written program for the statistical package R (www.r-project.org/) (R Development Core Team, 2004). Recordings were baseline corrected and normalized to the largest amplitude in the entire run. The relative peak amplitude and the onset of jaw opening were determined for each epoch separately. To assess the onset of jaw opening, the mean and standard deviation (SD) of the data points in the pre-instruction time window were calculated. Movement onset was defined as the time point at which the signal exceeded the mean value of the baseline ± 5 SD. The participants' vocal responses were recorded via the microphone channel of the Silent Scan Audio System (Avotec, Stuart, FL) and stored on a PC to monitor response accuracy.

3. Results

3.1. The neural circuitry of speech production in younger and older individuals

Overt speech production was associated with the activation of a distributed and bilateral neural network including the pyramidal and extrapyramidal motor system, both in younger and older individuals. Cortical activation related to the production of /a/ and /pataka/ compared to baseline is illustrated in Fig. 2 (red areas). Activation in the frontal and cingulate cortex included the medial prefrontal gyrus (supplementary motor area, SMA), the anterior cingulate gyrus (cingulate motor area, CMA), and the precentral gyrus (primary motor cortex) in both hemispheres. In addition, activation was present in the bilateral superior temporal cortex, the bilateral transverse temporal gyri (Heschl's gyri, primary auditory cortex), and the bilateral insular cortex. Subcortical activation included the thalamus, putamen, and the cerebellar hemispheres.

3.2. Age-related differences in the neural circuitry of speech production

A two-way ANOVA with the factors condition and age found significant main effects of age (young > old) in the

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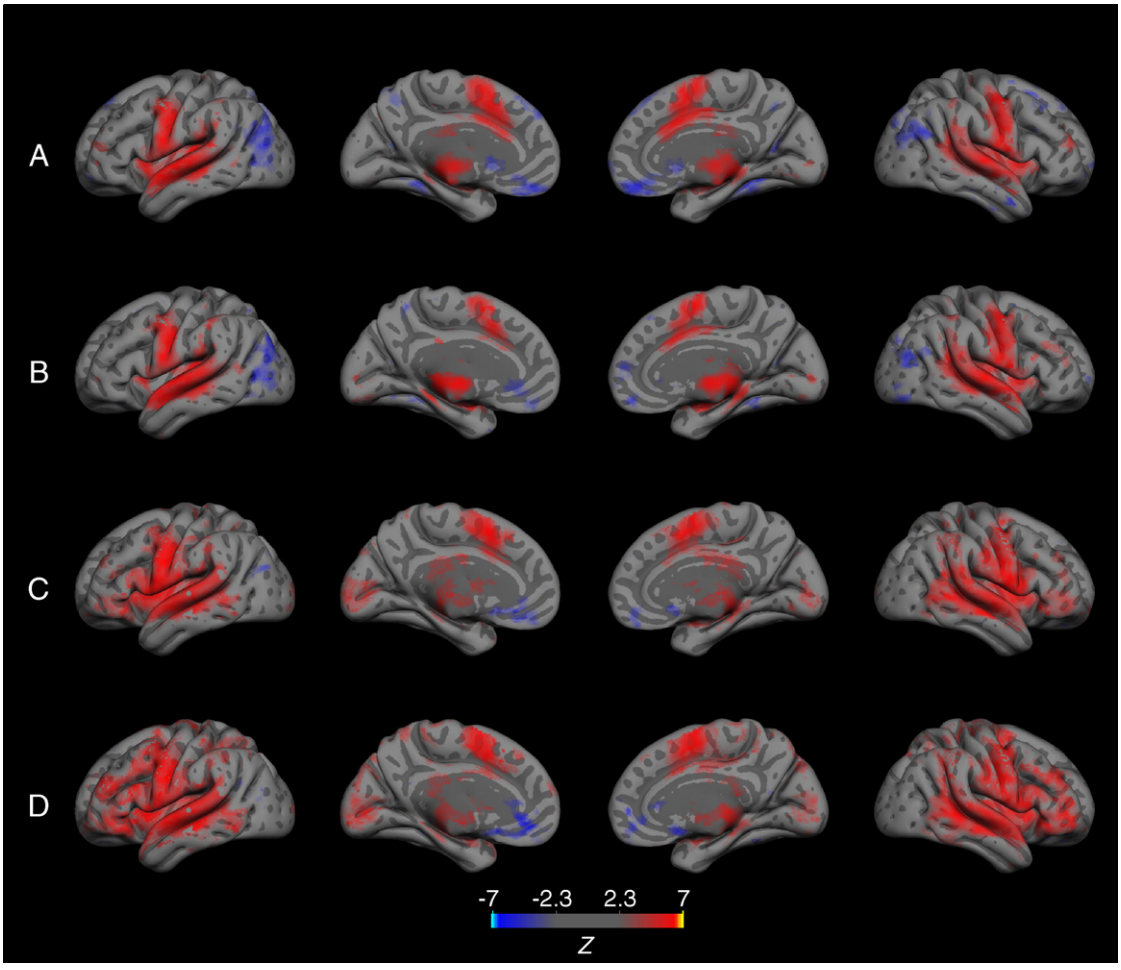

Fig. 2. Significant brain activation associated with the production of /a/ in younger individuals (A), /pataka/ in younger individuals (B), /a/ in older individuals (C), and /pataka/ in older individuals (D), vs. baseline. Activation maps are superimposed onto a 3D-reconstructed template brain (MNI 152). Task-related activation (red) is found in a bilateral network including the supplementary motor area, the anterior cingulate gyrus (cingulate motor area), the precentral gyrus, the superior temporal cortex, the transverse temporal gyrus, and the insular cortex.

bilateral posterior superior temporal cortex, posterior temporal plane, and transverse temporal gyrus (Fig. 3, red). Significant main effects of age (old > young) were found in the bilateral middle temporal gyrus, medial frontal gyrus, middle frontal gyrus, and inferior frontal gyrus (Fig. 3, blue). Table 1 summarizes the coordinates of the local activation maxima, the corresponding brain areas, and their *Z* values for the main effect of age. No significant main effects of con-

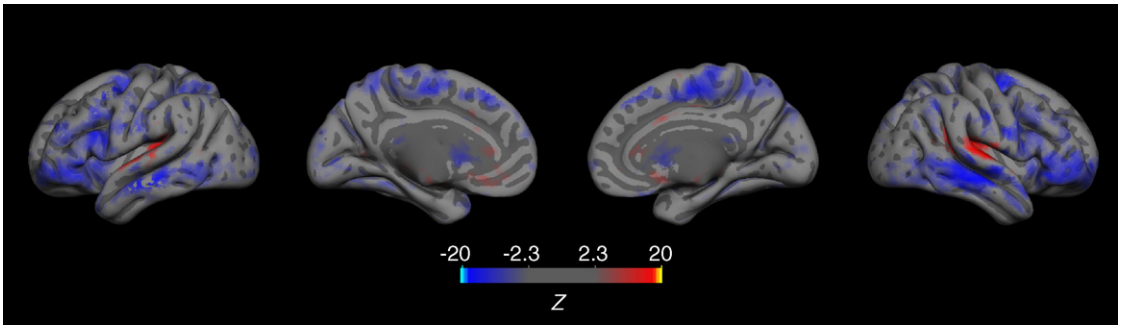

Fig. 3. Significant main effects of age. In younger compared to older individuals, significantly greater activation was found in the bilateral posterior superior temporal cortex, posterior temporal plane, and transverse temporal gyri, irrespective of the experimental condition (red areas). In older compared to younger individuals, significantly greater activation was found in the bilateral middle temporal gyri, medial frontal gyri, middle frontal gyri, and inferior frontal gyri (blue areas). Activation maps are superimposed onto a 3D-reconstructed template brain (MNI 152).

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Table 1
Stereotaxic coordinates of brain activation and corresponding brain areas associated with overt speech production in younger and older individuals (ANOVA, main effect of age).

Area of activation	BA	*x* (mm)	*y* (mm)	*z* (mm)	*Z* value	Volume (ml)
Young > old						
L superior temporal gyrus	41	−36	−30	14	13.18	0.16
R superior temporal gyrus	41	46	−32	14	20.88	0.45
L transverse temporal gyrus	41	−34	−28	12	13.35	0.16
R transverse temporal gyrus	41	46	−30	12	20.77	0.45
L insula	13	−58	−34	20	5.01	0.16
R insula	13	34	−30	14	19.62	0.45
Old > young						
L superior frontal gyrus	10	−24	58	−12	−7.9	4.8
R superior frontal gyrus	10	30	60	−10	−9.34	4.8
L middle frontal gyrus	6	−38	4	54	−10.96	4.8
R middle frontal gyrus	6	28	−4	58	−10.63	4.8
L inferior frontal gyrus	9	−46	18	18	−11.78	4.8
R inferior frontal gyrus	47	52	32	−10	−10.44	4.8
L medial frontal gyrus	6	2	−10	54	−10.39	4.8
R medial frontal gyrus	6	4	−8	54	−10.2	4.8
L precentral gyrus	6	−32	−2	54	−9.26	4.8
R precentral gyrus	6	56	−2	18	−10.77	4.8
L postcentral gyrus	3	−24	−34	54	−6.82	4.8
R postcentral gyrus	3	60	−14	34	−8.71	4.8
L superior parietal lobule	7	−34	−58	58	−7.03	4.8
R superior parietal lobule	7	12	−64	62	−6.43	4.8
L middle temporal gyrus	21	−68	−28	−10	−11.81	4.8
R middle temporal gyrus	21	64	−22	−10	−14.22	4.8
L inferior temporal gyrus	37	−62	−64	−12	−7.46	4.8
R inferior temporal gyrus	37	70	−50	−10	−6.75	4.8

Coordinates (in MNI space) identify the voxel with the highest local *Z* value. To determine local maxima, a *Z* value ≥ 2.3 and a minimum cluster size of 100 voxels (0.8 ml) were chosen. BA denotes Brodmann area.

dition and no significant interaction of age and condition were found.

3.3. Behavioral data

The behavioral performance during the fMRI experiment, represented by response latency and accuracy, was not significantly different between younger and older adults (data not shown).

4. Discussion

4.1. The neural circuitry of speech production in younger and older individuals

As expected, speech production in older individuals involves a complex network of motor control and phonological processing, similar to the brain activation found in our previous study that included only younger adults (Sörös et al., 2006b).

4.2. Effect of age: overactivation in older individuals

In older individuals, the bilateral medial frontal gyrus, inferior frontal gyrus, and middle temporal gyrus were significantly more active compared to younger individuals. The extent of age-related changes in brain structure and function is not similar across the entire brain, but varies between brain areas. Strong age-related reduction in white and grey matter as well as changes in connectivity and brain activation have been found in the prefrontal cortex (Rajah and D'Esposito, 2005). In the present study, activation of the bilateral inferior frontal gyrus was significantly stronger in older than younger individuals during the production of /a/ and /pataka/. Functional imaging studies have provided evidence that sub-regions of the left inferior frontal gyrus subserve, among other functions, phonological, semantic, and syntactic processing (Nishitani et al., 2005). Brodmann area (BA) 44, part of Broca's area, is also activated by the planning and programming of complex articulatory movements of oral and laryngeal musculature (Horwitz et al., 2003; Davis et al., 2008). Our results indicate that, in younger adults, the production of /a/ and /pataka/ does not necessarily involve Broca's area (Sörös et al., 2006b). The activation of the bilateral inferior frontal cortex in older adults whose behavioral performance in overt speech production was not significantly different from younger adults may be interpreted as compensation of age-related functional decline. The compensatory potential of the right (Crinion and Leff, 2007) and left inferior frontal gyrus (Sörös et al., 2003) has been established by functional brain imaging studies assessing the

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neural correlates of functional recovery after ischemic brain lesions.

In older individuals, overactivation was also found in the bilateral middle temporal gyrus. There is convincing evidence that parts of the left and, to a lesser extent, right middle temporal gyrus are involved in lexical and semantic access (Hickok and Poeppel, 2007) and language comprehension. Overt naming of semantically related word-picture pairs activated a left-lateralized network, involving the middle temporal gyrus, the inferior frontal gyrus, the superior frontal gyrus, and the angular gyrus (Mechelli et al., 2007). Data from stroke patients with left-hemispheric lesions and speech-language deficits indicate that auditory comprehension was most affected by lesions in the left middle temporal gyrus (Bates et al., 2003). Based on these findings, we speculate that overactivation in the middle temporal gyrus represents a shift of neural resources to compensate for the underactivation found in the superior temporal cortex (see below).

The supplementary motor area has been implicated in the programming, execution and control of fine, sequential movements (Dum and Strick, 2002). Activation of the bilateral SMA is a consistent finding in imaging studies on voluntary oro-facial movements, such as whistling (Dresel et al., 2005), chewing (Onozuka et al., 2002), tongue elevation (Martin et al., 2004), and swallowing (Sörös et al., 2009a). Increased activation of the SMA in healthy aging has been found in several studies involving simple (Mattay et al., 2002) and more complex movements (Wu and Hallett, 2005; Heuninckx et al., 2005). Overactivation of the SMA in our study on speech production and in previous studies involving pure motor tasks can be interpreted as an age-related shift from automatic to more self-initiated motor control (Heuninckx et al., 2005).

4.3. Effect of age: underactivation in older individuals

In older vs. younger participants, decreased activity was found in the bilateral transverse temporal gyrus and the bilateral posterior superior temporal cortex, key areas of cortical auditory processing (Lütkenhöner and Steinsträter, 1998). There is evidence that the left and right superior temporal cortex are involved in the processing of tones, music, and speech, although in a differential way. The left auditory cortex is supposed to be mainly involved in the processing of temporal features of sound, whereas the right auditory cortex is mainly involved in pitch processing (Zatorre and Gandour, 2008). Due to the design of the study, presenting an auditory cue immediately before the overt response, it is difficult to decide whether the decrease of activation in the superior temporal cortex merely reflects changes in auditory processing of the cue. A magnetoencephalographic study on the auditory processing of short sequences of the vowel /a/ suggested increased cortical evoked middle- and long-latency responses in healthy older participants (Sörös et al., 2009b). Thus, it appears unlikely that decreased activation in the primary and secondary auditory cortices in older individuals solely relates to an age-related decline in the cortical processing of sound.

There is convincing evidence that the left superior temporal cortex is involved in phonological processing. An fMRI study using data from an auditory pseudoword repetition task and a picture naming task with items of varying word frequency revealed significant activation of the posterior superior temporal gyrus in both independent experiments (Graves et al., 2008). In an fMRI study on covert naming with names consisting of one to four syllables, the left posterior superior temporal cortex was activated progressively, in relation to the word length, in all subjects during covert naming (Okada et al., 2003), suggesting that the shown superior temporal activity is, at least in part, due to phonological processing. In healthy aging, underactivation of the bilateral posterior superior temporal cortex and overactivation of the bilateral posterior middle temporal gyrus might indicate neuroplastic changes that are associated with a shift of neural resources dedicated to the retrieval of phonological information.

4.4. Effect of condition and interaction age × condition

No significant main effect of condition (/a/ vs. /pataka/), irrespective of the age group, and no significant interaction of age and condition were found. It has to be noted that in our earlier study, comprising a smaller ($n = 9$), but more homogeneous sample of healthy younger individuals (age range: 22–32 years), significant differences between conditions emerged. Production of /pataka/ vs. /a/ was associated with significantly greater activation of the bilateral superior temporal gyrus, bilateral middle temporal gyrus, left inferior temporal gyrus, left caudate, and the bilateral cerebellum (lobules VI, VIII, and IX) (Sörös et al., 2006b).

5. Methodological considerations

FMRI detects local task-related changes in cerebral blood oxygenation, closely reflecting the underlying neural activity (Logothetis et al., 2001). The interpretation of the presented results relies on the assumption that the close coupling between neural activity and the fMRI signal, convincingly shown for younger adults, is also true in older individuals, despite possible age-related changes in the vascular reactivity of the brain (Riecker et al., 2003; D'Esposito et al., 2003). Studies on the spatial and temporal characteristics of the hemodynamic response function indicated that the signal-to-noise ratio and the peak amplitude may decrease and the time-to-peak latency may increase in older vs. younger participants (D'Esposito et al., 2003; Rajah and D'Esposito, 2005), potentially resulting in a smaller number of significantly activated voxels. However, our results indicate that, at least in parts of the motor system, younger and older participants had a comparable hemodynamic response because no significant changes in activity were seen between age groups

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in the primary motor cortex, the SMA, and the cingulate motor areas. In addition, we found differential changes of the BOLD signal in various areas of the aging brain. Areas with increased BOLD signal in older individuals included the bilateral inferior frontal gyri and the left anterior insula, areas with decreased BOLD signal included the right superior temporal gyrus and the right basal ganglia. These findings provide strong evidence that our results represent age-related changes in neural function rather than generalized changes of cerebral blood flow or neurovascular coupling (D'Esposito et al., 2003; Fridriksson et al., 2006). To minimize the potential influence of vascular pathology on the fMRI results, we carefully selected all participants based on their medical history and T2-weighted brain scans.

Another issue is whether the small signal artefacts inevitably present within fMRI data differ between younger and older adults. Different artefact levels could potentially introduce bias into the interpretation of fMRI results. As expected (Seto et al., 2001), head movement, a major source of artifactual signal changes in fMRI, was significantly larger in older individuals in the present study. To minimize the effect of artifactual signal changes in the statistical analysis, functional data sets were decomposed in spatially and temporally independent components using independent component analysis (Beckmann and Smith, 2004). Artifactual components, mainly characterized by signal changes around the surface of the brain and the air-filled cavities, were then removed from the original data set by this procedure.

Clustered image acquisition provided us with a silent window of about 8 s in which the auditory cue was presented and the overt response was made without interference by the acoustic noise produced by the MRI scanner. This technique, however, only presents a snapshot of brain activity rather than the temporal course of the hemodynamic response. Thus, it is not possible to determine whether decreased superior temporal activity in older individuals is due to a reduction or a delay in the BOLD hemodynamic response. However, it should be possible to answer this question in the future, for example by manipulating the time delay between clustered acquisition and overt response.

Disclosure statement

All authors disclose no actual or potential conflicts of interest.

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